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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/846,606	04/30/97	RAVNIKAR	P JB06000

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HM11/0414

EXAMINER

RAILEY, J

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 04/14/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

08/846,606

Applicant(s)

Ravnikar et al.

Examiner

J. Railey

Group Art Unit

1636



☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-13 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-13 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☒ The proposed drawing correction, filed on 30 Mar 1998 is ☒ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 1 & 5

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yasukawa et al. [J. Biol. Chem. **270**(43):25328-25331 (1995)] taken in view of LaVallie et al. [Bio/Technology **11**:187-193 (1993)].

Yasukawa et al. teach the transformation of *E. coli* with separate plasmids for the

production of soluble foreign proteins. One plasmid encodes the foreign protein, and the second plasmid encodes the *E. coli* thioredoxin gene. The co-expression of the foreign protein with the thioredoxin protein in the host cell results in a large increase of soluble foreign protein produced, versus host cells which express only the foreign protein without thioredoxin. See Figure 2, for example. In the Discussion, Yasukawa et al. refer to the reference by LaVallie et al. [Bio/Technology 11:187-193 (1993)] as citation number (27) and note that their system is superior to that of LaVallie et al. in that the thioredoxin protein is not expressed as a fusion protein with the foreign protein. This allows for the overproduction of free thioredoxin protein within the cell, which increases the solubility of the foreign protein, yet the thioredoxin does not have to be cleaved from the foreign protein by the action of a specific peptidase. The Discussion notes that this arrangement is "a big advantage in the preparing the large amounts of proteins for structural studies." LaVallie et al. is cited to note that both the thioredoxin and the foreign protein can be expressed from the same plasmid and not necessarily from separate plasmids.

Applicant claims vectors which contain both the thioredoxin gene and a gene encoding a heterologous protein. These vectors are introduced into bacteria, preferable *E. coli* for the production of large amounts of soluble foreign protein which is not fused to the thioredoxin protein. Applicant claims bacteria transformed with this vector and methods of producing soluble heterologous protein in bacteria. The difference between what applicant claims and the teachings of Yasukawa et al. is that Yasukawa et al. teach the co-transformation of separate plasmids into

E. coli for the separate production of the thioredoxin and the heterologous protein within the host cell, while applicant teaches the co-expression of these proteins from genes found separately on the same plasmid. Absent evidence to the contrary, the co-expression of separate genes on the same plasmid would have been obvious given the combined teachings of the prior art. It has been well established in the art that several genes can be expressed on the same plasmid from the same or different promoters. For example, both references teach plasmids in which selectable markers for antibiotic resistance are co-expressed in each plasmid along with other genes of interest. Also, as noted in the Discussion of Yasukawa et al., a plasmid co-expressing thioredoxin and the *E. coli* heat shock chaperone GroE could be done from the same plasmid. Consequently, the co-expression of both the thioredoxin gene and a foreign gene of interest from the same plasmid would have been obvious.

If applicant provides a declaration under 37 CFR §1.131 to overcome the cited publication by Yasukawa et al., the instant application will be suspended pending a potential interference. Ishii et al. [EP 0 768 382 A2] is provided as of interest.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Art Unit 1636 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for Art Unit 1636 is (703) 308-4242 or 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. F. Railey, whose telephone number is (703) 308-0281. The examiner can normally be reached on Monday-Thursday, and alternate Fridays, from 8:00 AM-5:30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached at (703) 308-4003. The fax phone number for informal transmissions to the examiner is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13 April 1998

JOHNNY F. RAILEY II, PH.D.
PATENT EXAMINER
GROUP 1630

John F. Railey II